

Understanding Between-Person Interventions With Time-Intensive Longitudinal Outcome Data: Longitudinal Mediation Analyses

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Abstract

Background Mediation analysis is an important tool for understanding the processes through which interventions affect health outcomes over time. Typically the temporal intervals between X, M, and Y are fixed by design, and little focus is given to the temporal dynamics of the processes.

Purpose In this article, we aim to highlight the importance of considering the timing of the causal effects of a between-person intervention X, on M and Y, resulting in a deeper understanding of mediation.

Methods We provide a framework for examining the impact of a between-person intervention X on M and Y over time when M and Y are measured repeatedly. Five conceptual and analytic steps involve visualizing the effects of the intervention on Y, M, the relationship of M

and Y, and the mediating process over time and selecting an appropriate analytic model.

Results We demonstrate how these steps can be applied to two empirical examples of health behavior change interventions. We show that the patterns of longitudinal mediation can be fit with versions of longitudinal multi-level structural equation models that represent how the magnitude of direct and indirect effects vary over time.

Conclusions We urge researchers and methodologists to pay more attention to temporal dynamics in the causal analysis of interventions.

Keywords: Longitudinal mediation · Multilevel mediation · Temporal dynamics · Health behavior change interventions · Between-person intervention · Intensive longitudinal data

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Research in health and behavioral sciences strives to understand the causal mechanisms affecting human experience and behavior. For this purpose, randomized experimental designs are the gold standard for evidence, as they isolate the effect of an intervention from various possible confounding processes. However, the interpretation of the obtained effect may be subject to debate, and so researchers often test intervening mechanisms by carrying out a mediation analysis. Mediation describes a causal process that unfolds over time [1–4]. In its simplest form, it represents an intervention (X) causing a change in a mediator (M), which then causes change in an outcome (Y). Following Baron and Kenny [1], the path $X \rightarrow M$ is typically referred to as the *a* path, and the path $M \rightarrow Y$ is typically referred to as the *b* path. Adjusting for M, the direct (unmediated) path between X and Y is referred to as the *c'* path (see Fig. 1).

Causal analysts emphasize the causal ordering of X, M, and Y [5], with X preceding and causing M and M preceding and causing Y. But rarely do they focus on the temporal dynamics of these processes (e.g., [6,7]). Are the impacts of X and M immediate or do they take time to develop? How long do the causal effects of X and M last? Are the temporal dynamics for $X \rightarrow M$ and $M \rightarrow Y$ the same? Cole and Maxwell [8,9] showed that incorrect temporal assumptions about sequences of X, M, and Y processes can lead to inconsistent and biased results. To date, however, researchers have not been given a framework for understanding which temporal assumptions are appropriate. In this paper, we aim to draw researchers' attention to the importance of considering temporal dynamics in mediation processes following an intervention. To make this point, in Fig. 1, we explicitly added time to the classic mediation model.

In most interventions, time is treated as a fixed parameter rather than a dimension to be analyzed. Researchers who design and register randomized trials must specify how long to wait to measure the primary outcome following the intervention, and the interval length may or may not be explicitly justified. Depending on the outcome and field (e.g., health, clinical, and educational interventions), there may be conventions for specifying whether the outcome interval is 1 month, 6 months, or some other interval.

Often, researchers assess outcomes at multiple times. Multiple assessments allow the mediating process to be measured prior to the outcome. When designs have multiple time points for the outcome and mediating processes, we label them longitudinal mediation designs. A special case of longitudinal mediation designs is one that uses intensive longitudinal data. These might be daily accelerometer measurements following a physical activity intervention [10], ecological momentary mood assessments following a clinical intervention [11], or ambulatory blood pressure monitoring in a medical trial [12]. Over the past decade, there has been a sharp increase in the numbers of studies using intensive longitudinal data [13]. With technological advances, studying psychological, behavioral, and physiological processes

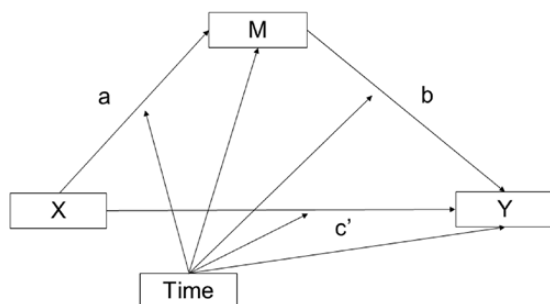


Fig. 1. The Baron and Kenny [1] mediation model, expanded to represent potential temporal effects in the mediation process.

has become accessible, and researchers seem to recognize the unique value of such data. We argue that collecting longitudinal data, especially intensive longitudinal data, following a between-subjects randomized intervention offers important advantages over traditional mediation designs.

In this article, we provide a framework for how to assess and better understand the temporal dynamics of a between-person intervention. Very few modeling approaches have proposed solutions for mechanisms of between-person interventions, a case that is very important for behavioral medicine. The framework should serve as a flexible tool encouraging researchers to think about the temporal dynamics of causal intervention effects when designing interventions and choosing appropriate statistical models. To keep the exposition relatively simple, we limit our discussion to models with only one mediating process, but the principles we discuss can be extended to more complex mediation models.

We propose five conceptual and analytic steps: (a) examine the intervention effects on outcomes at different time points; (b) examine intervention effect on hypothesized mediator at different time points; (c) examine the relation of the mediator to the outcome at different time points; (d) determine if there is temporal variation in the mediating process; and (e) fit an appropriate analytic model that matches the patterns described in the first four steps.

The first four steps implicitly acknowledge that a between-person intervention can have different causal effects over time on the outcome and the mediator. Figure 2 illustrates four of many possible causal patterns for an intervention at Time 0 that all end up at the same point seven temporal units later. The bottom

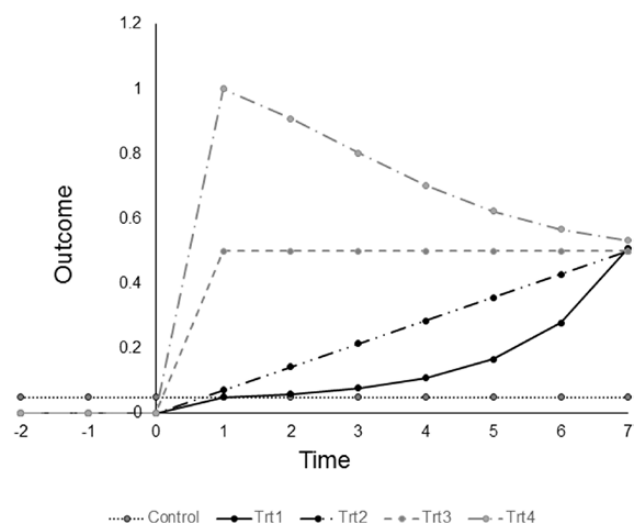


Fig. 2. Examples of four temporal patterns of change following an intervention (trt = treatment vs. control) that is administered at Time 0. All five end up at the same level at Time 7.

pattern (Trt1) exponentially builds up its effect, the second (Trt2) builds its effect linearly, and the third (Trt3) has an immediate and constant effect. The fourth (Trt4) has a large immediate effect and then gradually declines. Sometimes, such patterns can be anticipated theoretically before the study is initiated, and other times the investigator may discover the pattern after having collected longitudinal data.

In the next section, we describe the logic of each of the five steps. Note that Steps 1–4 are descriptive. Step 5 can be approached analytically in many ways. We briefly review different statistical approaches. Following this overview, we show how these steps would apply to two empirical examples of health behavior change interventions and we present one way of modeling that illustrates the logic of the approach. Both studies implemented intensive longitudinal methods (e.g., daily electronic diaries) that allow the description and analysis of the temporal dynamics in outcomes and mediating processes [10,14,15]. The first of these is a between-person randomized trial of a support group intervention to promote healthy eating, with seven assessments of a mediator and the outcome, both quantitative measures. The second is a between-person randomized trial of an action control text message intervention

to promote meeting daily activity recommendations. Although the proposed mediator is measured as a quantitative process, the outcome (goal attainment) was a binary response.

Step 1: Examine the Intervention Effects on Outcomes at Different Time Points

With intensive longitudinal data, it is possible to represent the outcome levels in the intervention and control groups for many time points graphically, as well as the difference of the two groups. This gives an important indication whether intervention effects are unfolding abruptly, increasing continuously, or decreasing after some time (including curvilinear dynamics). Such a graphic display also reveals the temporal dynamics of the control group. Figure 3 shows two versions of graphical displays for each of the two empirical examples, which will be discussed in detail below. After creating the display for each group, the researcher can make decisions about appropriate mathematical models to represent the average trajectories over time.

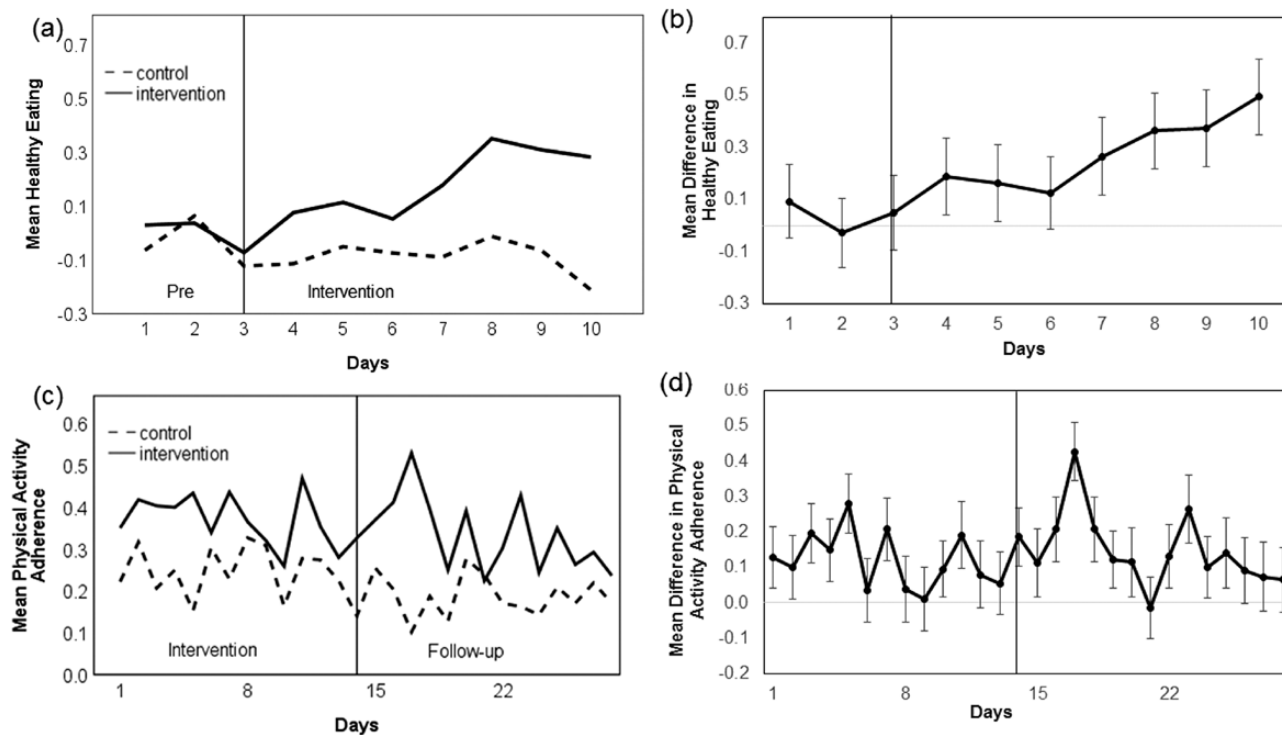


Fig. 3. Example 1: (a) mean healthy eating in the intervention and control group over the study days (pre: before the intervention, and during the intervention phase); (b) mean differences (and standard errors [SEs]) in healthy eating between control and intervention group. Example 2: (c) mean physical activity adherence in the intervention and control group over the 14 days of intervention and 14 days following intervention; (d) mean differences (and SEs) in physical activity adherence between control and intervention group.

Step 2: Examine Intervention Effect on Hypothesized Mediating Process at Different Time Points

Similar to the effects on the outcome of an intervention, the effect of the intervention on mediating mechanisms may depend on time. So again, it is possible to represent the mediator levels in the intervention and control groups for many time points graphically, as well as the difference of the two groups. The examples we will discuss in detail are illustrated in Fig. 4. Again, the temporal trends will inform what mathematical models are appropriate for accounting for change over time.

Step 3: Examine the Relation of the Mediator to the Outcome at Different Time Points

Besides the temporal effects of the intervention, there may also be variability in how the mediator affects the outcome over time. Researchers may thus be interested in understanding if a mediator becomes more effective over time or if and when a mediator's effect on an outcome decreases. In contrast to the first two steps in the analysis, the temporal dynamics of the association of the mediator and the outcome cannot be observed directly. One way to explore the dynamics is to compute

the between-person association of the mediator and the outcome for each time point separately and plot these. Another way is to examine, for each person, the correlation of the mediator and the outcome over time points. Because the former is more comparable to Steps 1 and 2 than the latter, in this article, we focus on the between-person correlations. An illustration of this is shown in Fig. 5 and will be discussed below.

Step 4: Determine if There is Temporal Variation in the Mediating Process

In addition to temporal variations in a and b paths separately (Steps 2 and 3), the importance of the mediating process might also vary over time. For example, a mediator might be more important in the beginning of an intervention and then fade over time. This might occur because participants become less engaged with the intervention or because other processes (such as habit formation) begin to explain the intervention effect on the outcome at later times. In Step 4, we are thus interested in investigating at what time a mediating process is explanatory for the intervention effect on the outcome. For this purpose, we recommend computing and graphing the total and

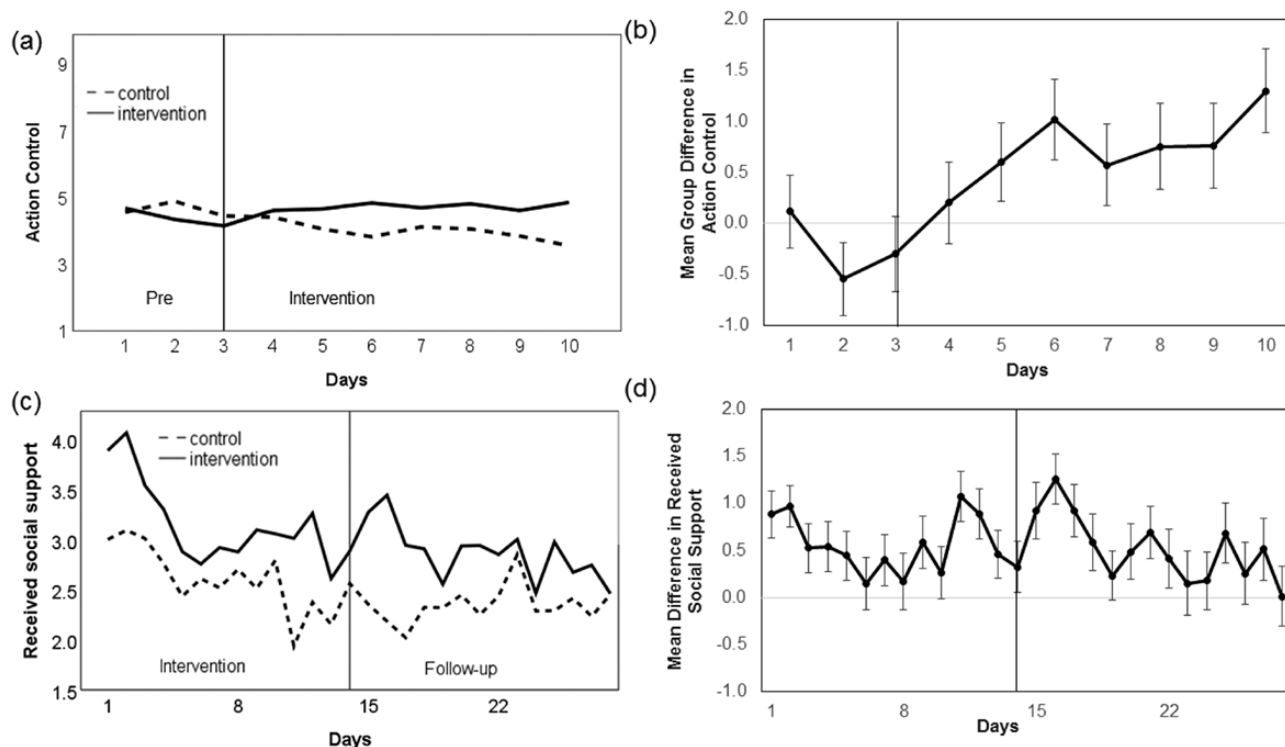


Fig. 4. Example 1: (a) mean action control in the intervention and control group over the study days; (b) mean differences (and standard errors [SEs]) in action control between control and intervention group. Example 2: (c) mean received social support in the intervention and control group over the 14 days of intervention and 14 days following intervention; (d) mean differences (and SEs) in received social support between control and intervention group.

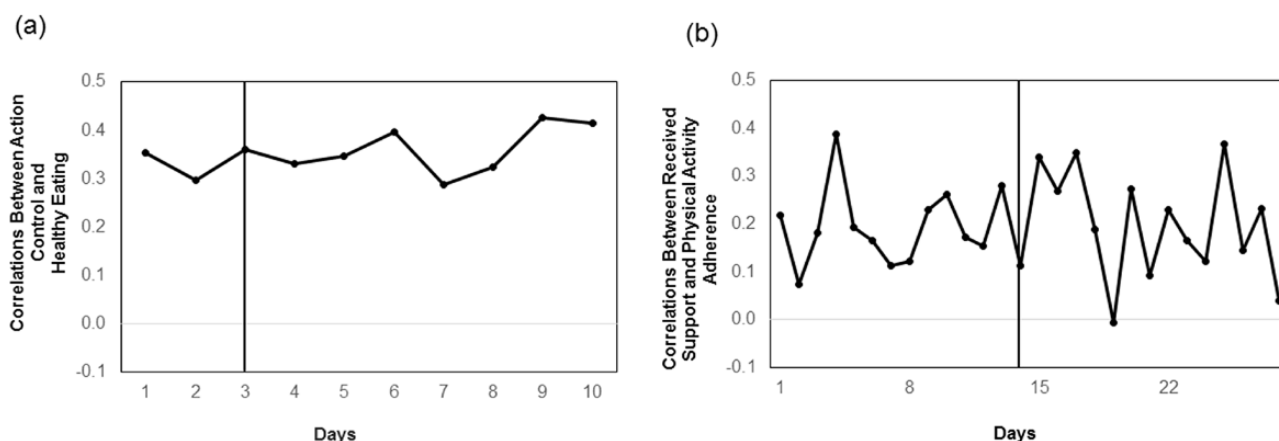


Fig. 5. (a) Example 1: correlations of the mediator action control and healthy eating. (b) Example 2: correlations of the mediator received support and physical activity adherence.

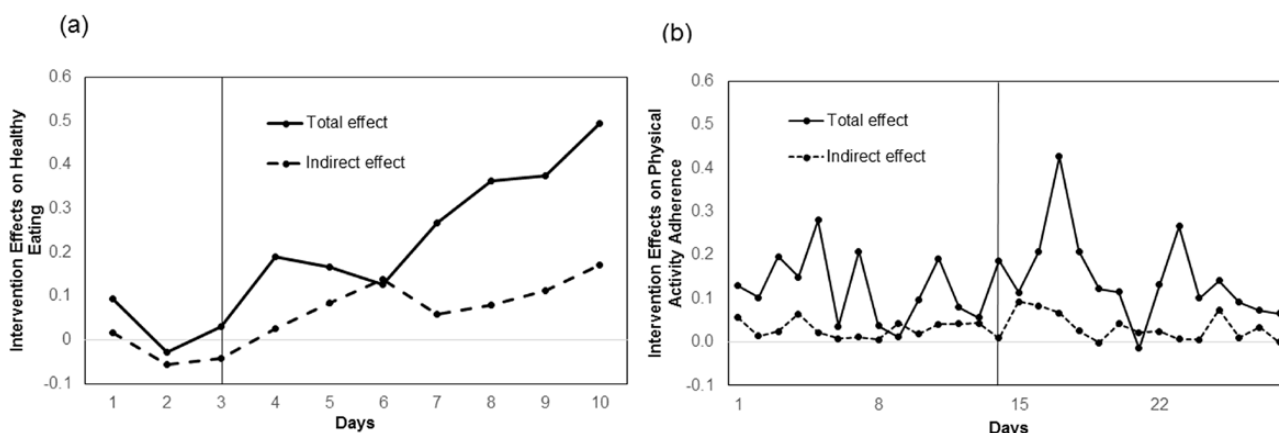


Fig. 6. (a) Example 1: total and indirect effects of the intervention on healthy eating. (b) Example 2: total and indirect effects of the intervention on physical activity adherence, represented using a probit link function.

indirect effects of the intervention. This gives an overview of the variability of the mediating mechanism over time. Figure 6 shows graphs of temporal variability for the two examples that we will discuss in more detail below.

Step 5: Select Appropriate Analytic Model

Steps 1–4 can provide valuable insights into the temporal dynamics of the effects of an intervention administered in a randomized trial on both the outcome and the hypothesized mediator. The final step of longitudinal mediation is fitting appropriate multivariate statistical models that take into account all the temporal data. The usual approach when applying longitudinal mediation models is to identify the most theoretically plausible model and apply that model [16]. In this article, we focus on designs where the intervention is a constant between-person manipulation, and the mediator and outcome are possibly time-varying within person following the administration

of the manipulation or the control. Such models have been called 2-1-1 models [17], where 2 represents a higher-order effect and 1 represents the effects on the lower level. In the longitudinal context, the higher-order levels are persons and the lower-order effects are times within person. We focus on an intent-to-treat analysis, where the treatment status is considered fixed regardless of compliance with the intervention.

The statistical models that are appropriate for modeling trajectories of the mediator and the outcome in the treatment and control groups are a subset of a large set of models that have been proposed as longitudinal mediation models. Many of the existing models treat X , the causal intervention, as time-varying within person, rather than as a between-person experimental manipulation. These are called 1-1-1 models [17], where all three components of the mediation process are at the time-varying level. An example of a 1-1-1 design is time-varying self-reported mother hostility (X), self-reported maternal supportive behavior (M), and child-reported hostility (Y) [18]. Important examples of 1-1-1 models are models for panel data described by Maxwell et al.

(e.g., [8,9]) and by O’Laughlin et al. [18] and the Granger-mediation models described by Zhao and Luo [19] for fMRI data. Because these are not designed for the 2-1-1 framework, and they introduce extraneous complications to our approach, they will not be discussed further.

There are many possible approaches to the analysis of longitudinal trajectories of the mediator and outcome in a 2-1-1 model, including multilevel models [17], latent growth models [20], multilevel structural equation models (MSEMs) [21], and MSEMs with autoregressive components [22]. Variations of the approaches include Bayes estimation, as well as maximum likelihood methods [23]. It is beyond the scope of this article to review the details of all these approaches. Which method is most appropriate for a given research problem depends on the nature of the mediating and outcome processes, as well as the nature of the available data. Models that represent 2-1-1 longitudinal mediation designs must consider a number of features of the process. These include the four initial steps of our framework. In addition, researchers should consider the nature of the longitudinal processes and the available data. For example, does the level of the mediator and outcome at each time point affect the levels of these processes at the next time point as a structural dynamic process? If so, vector autoregressive models may be appropriate [24], as well as sequential mediation models [25]. How many time points are measured following the introduction of the intervention? Intensive longitudinal designs should have at least seven temporal measurements (cf., [26]) but, in randomized trials, there are often as few as three. While this restricts the complexity of the longitudinal models one can fit, even three available time points can be examined using our conceptual steps. Does the timing of the repeated observations correspond to the dynamics of the longitudinal processes? If the mediator changes on a daily basis, are the measures also taken every day? What is the relative importance of between-person processes (such as differences in person-specific slopes) to within-person processes (such as responsiveness to time-specific events)? A final consideration is whether the data to be analyzed have patterns of missing data that are inconsistent with missing completely at random or missing at random [27]. In the next two sections, we illustrate the proposed steps with the two empirical examples introduced earlier and demonstrate the analytic decisions in the context of the considerations outlined above.

Empirical Example 1: Healthy Eating

Example 1 is a randomized trial of support groups to promote healthy eating where support was provided via smartphones [14]. In the intervention group, 100 participants supported each other in smartphone-based chat groups to reach a randomly assigned eating goal and completed daily diaries. In the control group, 103 participants filled in the electronic diaries only. Participants reported their food consumption and social-cognitive variables during three preintervention and seven intervention days. Several social-cognitive variables were registered as potential mediators of the intervention effect (see <https://osf.io/dsghj>). In the present paper, we focus on results involving action control [28]. This concept encompasses a person’s awareness of behavioral goals, self-monitoring of their behavior, and regulatory effort when encountering goal-behavior discrepancies [28]. It was measured with three items, one for each of the subfacets: awareness of standards (healthy eating goals), self-monitoring (observing one’s food consumption), and regulatory effort (regulating discrepancies between eating goals and food consumption). It was hypothesized that support messages promote healthy eating while they are being perceived, or perhaps up to a few hours after, for example, by reminding people of their healthy eating goals. The daily food consumption outcome was quantitative and was standardized to have mean 0 and variance 1. The data used in this example did not have missing data for the seven daily data points.

Step 1: Examine the Intervention Effects on Outcomes at Different Time Points

In Example 1, intervention and control groups had similar levels of healthy eating prior to the onset of the intervention (Fig. 3a). In the intervention period, there is a slight decline in healthy eating in the control group, whereas the intervention group’s healthy eating steadily increases. This gradual increase in the intervention effect on healthy eating over time is even more clearly visible in Fig. 3b, which displays the mean between-group differences in healthy eating for each time point. The visual impression is consistent with formal analyses using mixed models [14]. There was a main effect of the intervention, indicating that intervention participants consumed approximately 1.5 fruit and vegetable portions more or 0.75 unhealthy snacks less than control participants on the last day of the intervention phase. Furthermore, there was a gradual increase in the intervention effect over time and no evidence for a discrete jump [14].

Step 1 applied to Example 1 reveals the important insight that the effectiveness of smartphone-based support groups consisting of virtual strangers unfolds slowly

over time rather than abruptly showing large effects (e.g., due to effects of support expectancy).

Step 2: Examine Intervention Effect on Hypothesized Mediating Process at Different Time Points

In Example 1, the mediator is daily action control. There is a small decline in the control group over time, whereas action control slightly increased in the intervention group (see Fig. 4a). Figure 4b shows that the difference between the groups grows following the intervention steeply increases in the first 3 days and less steeply in the last 4 days. For Example 1, the intervention effect on the hypothesized mediator seems similar to its effect on the outcome as revealed in Step 1.

Step 3: Examine the Relation of the Mediator to the Outcome at Different Time Points

In Example 1, the association of the hypothesized mediator action control and healthy eating remained relatively stable over time (see Fig. 5a). It seems that stronger action control was similarly beneficial for healthy eating across the study period.

Step 4: Determine if There is Temporal Variation in the Mediating Process

In Example 1, the mediating process of action control varied over the course of the intervention period (see Fig. 6a). The total effect of the intervention indicates the increasing effectiveness of the intervention to promote healthy eating over time (consistent with the findings of Step 1). The indirect effect for action control, in turn, shows that this mechanism accounted for a larger proportion of the intervention effect at the beginning rather than later in the intervention phase. This could indicate that indeed automatic processes (e.g., habituation) might have become more important than effortful action control processes over the course of the intervention.

Step 5: Select Appropriate Analytic Model

The first four steps suggest that linear models can be used to represent the temporal trends of both the outcome, healthy eating, and the mediator action control. The intervention groups appear to differ over time on the rate of change of both processes and, hence, the appropriate model should represent group by trajectory interactions. The change in the indirect effect on Day 6, however, might be accounted for by the group differences in the mediator.

Two different classes of dynamic processes might account for the patterns observed for both the mediator and outcome. One is that the intervention creates a shared reality that it is possible to regulate healthy eating successfully. This could lead to a growth trajectory that is best represented as a person-specific slope. The other is that the level of healthy eating on a given day has a direct effect on the successful healthy eating of the next day. These alternate formulations reflect the between-person/within-person distinction discussed by Curran and Bauer [29].

Although the seven measurements in Example 1 are more than what are available in many randomized trials, the number is less than what is needed to have a clear picture of both trajectories and autoregressive dynamics (e.g., [22]). The total sample size of participants, however, was large enough to yield stable estimates of the between-person effects. For this reason, we illustrate the analysis representing the patterns shown in Steps 1–4 using an adaptation of the MSEM model of Preacher et al. [21]. The adaptation incorporates temporal effects represented in Fig. 1. We call this adaptation a longitudinal MSEM (LMSEM). Like conventional structural equation models, the method allows an explicit representation of direct and indirect paths. Like multilevel models, the method allows the within-person processes to vary across participants. In addition, the models incorporate time as a within-person process that can interact with the a , b , and c paths. LMSEM is related to dynamic structural equation models (DSEM) described by McNeish and Hamaker [22], but it does not account for possible autoregressive structures over time.

The LMSEM model was fit with Mplus using a two-level random effects specification and robust maximum likelihood estimation. The within-person component of the model specified possible time effects on the mediator (action control) and on the outcome (healthy eating) and within-person effects of the mediator on the outcome on the same day. All three of these were allowed to vary over subjects as random effects. The between-person component of the model specified possible treatment effects on the mediator and on the outcome, as well as treatment effects on the temporal slopes on both the mediator and the outcome. The indirect effect was calculated using the average within-person effect of the mediator on the outcome. No contextual effect was found [30]. The first day of the intervention was coded as 0. Bootstrap estimates of the indirect effects are not available with this specification, and so the significance test of the indirect effect is based on a t -test using a large sample standard error (SE). Because this test does not take into account the skew of the sampling distribution of the indirect effect estimates, it often is conservative [31]. The formal set

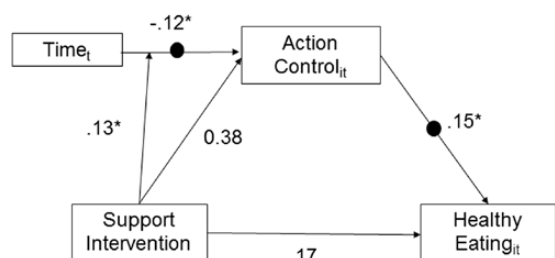


Fig. 7. Example 1. Longitudinal multilevel structural equation mediation model of between-person intervention on action control and healthy eating showing both interactions of support and time on action control and random effects (black dots on paths). i = individual, t = time.

of equations of this model, as well as the data and Mplus syntax implementing the analysis, can be found at <https://osf.io/7vbeh/>.

Figure 7 illustrates a simplified LMSEM representation of the data from Example 1. The subscripts in each box indicate if the variable is time varying (t), person varying (i) or both time and person varying (it). The arrows represent the direct effects. If the arrow is marked with a black dot, the fixed effect is the average of within-person random effects. The model posits that the support intervention has an impact on healthy eating on Day t and that it is partially mediated by action control on Day t .

Consistent with the visual inspection in Steps 1–4, there was a significant negative decrease in action control over time in the control group ($B = -0.12$, $SE = 0.05$, $p = .018$). Compared to the control group, in the intervention group, action control remained stable over time ($B = 0.13$, $SE = 0.06$, $p = .037$). The between-group difference in action control was not significant on the first day of the intervention ($B = 0.38$, $SE = 0.34$, $p = .269$), but higher action control was significantly associated with healthier eating that day ($B = 0.15$, $SE = 0.02$, $p < .001$). The indirect effect on the first day was not significant ($B = 0.06$, $SE = 0.05$, $p = .279$), but it significantly increased day by day ($B = 0.02$, $SE = 0.01$, $p = .044$). We used chi-square difference tests to investigate different models of how time influenced the results. For example, additionally accounting for temporal effects in the direct effect of the intervention on healthy eating did not further improve model fit (see <https://osf.io/7vbeh/>).

Conclusions

In Example 1, we learned that the outcome and the mediating process (action control) both increased gradually over the course of an intervention to increase healthy eating. The model suggested that the mediating effect of action control gradually increased over time while not significantly mediating intervention effects in the beginning. Thus, considering temporal patterns in mediation effects using intensive longitudinal data

were highly relevant for Example 1. This pattern is interesting, but it might be accounted for by an alternate statistical model that includes an autoregressive structure that implies that action control is dynamically drawn to a homeostatic set point rather than being driven by a steady increase in the treatment group. Another alternate model would include lagged effects of action control on one day and healthy eating the next, but this model is inconsistent with our theoretical model of action control effects. Thus, the longitudinal approach allows researchers to pose new interesting questions, as well as to consider summaries of available data.

Empirical Example 2: Physical Activity

Example 2 is a randomized trial of a text message intervention to promote couples' physical activity [10,15,32]. In the intervention group, 60 participants received an information leaflet, a goal-setting task, and daily text messages directly targeting their action control for 14 consecutive days. In the control group, 61 participants received the information leaflet and reminder messages to fill in the daily diaries. For 28 days (14 days of intervention and 14 days following intervention), participants' physical activity levels were assessed using accelerometers. The dyadic action control intervention was expected to be mediated by received support from the partner (controlled-trials.com, ISRCTN15705531), which was assessed every evening during the 28 days using an electronic diary. It was hypothesized that text message reminders promote better daily adherence to physical activity recommendations through specific supportive behaviors that same day. The daily outcome was a binary record of whether recommended activity was achieved. The median of available data points per person was 28. Randomization check based on baseline panel data confirmed comparability of the intervention and control group in terms of received support from the partner and self-reported physical activity.

Step 1: Examine the Intervention Effects on Outcomes at Different Time Points

Example 2 illustrates a very different temporal dynamic of intervention effects compared to Example 1. Right from the onset of the intervention, there is greater adherence to physical activity recommendations in the intervention compared to the control group, and this effect is sustained across the 14 days of intervention and 14 days following the intervention (see Fig. 3c). This is despite day-to-day fluctuations in the intervention effect (see Fig. 3d) that could be because individuals

often exercise on alternating days. In both groups, physical activity adherence steadily declines over time, and there is no observable difference in the rate of decline in the intervention group compared to the control group. The visual impression is consistent with formal analyses using mixed models [10]. At the onset of the intervention, intervention participants showed a higher probability of adhering to recommended physical activity levels (36.5%) compared to the control condition (23.0%) [10]. Over time, physical activity adherence declined significantly in both groups.

Step 1 applied to Example 2 reveals that the effect of this couple-based intervention successfully promotes physical activity from Day 1. The levels of the two conditions can be adequately summarized by two relatively smooth lines. The temporal analysis using intensive longitudinal data uncovered this important information that would have been lost using a traditional before–after trial design.

Step 2: Examine Intervention Effect on Hypothesized Mediating Process at Different Time Points

In Example 2, the mediator is received support [32]. Figure 4c shows that received support was higher in the intervention group than in the control group at the onset of the intervention and that this effect was generally sustained across the 14 day intervention phase and the 14 days following the intervention. Again, there are day-to-day fluctuations in how much the intervention affects received support (see Fig. 4d). Both groups' support showed relatively parallel trajectories over the course of the study, including the initial 3 days when received support was elevated in both groups and then declined slightly. In conclusion, the intervention effects on support seem immediate and persistent over the course of time, similar to the intervention effects on the outcome.

Step 3: Examine the Relation of the Mediator to the Outcome at Different Time Points

In Example 2, the correlations between received support and physical activity adherence fluctuated mostly between .1 and .4 but did not systematically change over time (see Fig. 5b). Overall, higher received support was associated with higher physical activity adherence.

Step 4: Determine if There is Temporal Variation in the Mediating Process

In Example 2, both the total and indirect effects of the intervention vary from day to day, but neither shows an overall time trend across the intervention and follow-up

phase, for example, increasing or decreasing over time (see Fig. 6b). The mediating process via received support seems to be relatively stable over time. This might suggest that, on days with higher intervention effectiveness, other mediators come at play. Because physical activity adherence was a binary variable, we computed total and indirect effects using a probit model as implemented in Mplus.

Step 5: Select Appropriate Analytic Model

In Example 2, we observed, in Steps 1–4, relatively stable levels of the outcome (adhering to physical activity levels) and the mediator (received support), although there was some decline over time. There were also no systematic patterns of change in how the intervention affects physical activity adherence (*c* path), received support from the partner (*a* path), or how received support affects adherence (*b* path) over time. Instead, we found instantaneous effects of the intervention on physical activity adherence and support from the onset of the intervention that remained stable across the 14 days of intervention and 14 days following the intervention. This may be attributable to the nature of the intervention, with some components (e.g., information leaflet and goal setting) being delivered only once at the beginning of the intervention phase and other components (e.g., text messages) delivered repeatedly (one text per weekday) across a period of 2 weeks.

As in Example 1, the patterns revealed in the Steps 1–4 for Example 2 could be represented by a version of the longitudinal multilevel structural equation approach described above. This approach allows trajectories of physical activity adherence and amount of received support over time to be modeled at the within-person level and for these effects to vary across participants (random effects). It also allows for the within-person association of received support and likelihood of adhering to the physical activity levels over days. At the between-person level, the effect of the intervention can be assessed for the overall level of social support and physical level adherence, as well as the degree of changes in the mediator and outcome over time. From Steps 1–4, we anticipate that a good statistical model for Example 2 will not involve many interactions with time, as the patterns seem to be consistent over time. Because Example 2 includes 28 time points, there is also enough information to adjust for possible autoregressive patterns in the residuals of the mediator and outcome. This extension of the LMSEM model of Example 1 was called a residual DSEM (RDSEM) by McNeish and Hamaker [22].

One feature of Example 2 that is more complicated than Example 1 is that the outcome is binary: adhering to physical activity levels versus not adhering. Fortunately, RDSEM methods include link functions from generalized linear models that allow binary outcomes to be modeled as if they were quantitative. Usually there is a choice between a logistic link and a probit link but, in the context of a mediation analysis, the probit link is clearly the better choice. MacKinnon and Dwyer [33] have shown that the sum of the indirect effect and the direct effect does not equal the total effect when the binary outcome is modeled with a logistic link function. The probit link function, on the other hand, allows the mediation analysis to be interpreted much like a mediation analysis with a quantitative outcome. Out of this reason, we thus chose the probit link in the RDSEM model in our example.

The RDSEM model we used adjusted for the effect of time on received support and on physical activity adherence and specified these temporal trends as random effects, allowing for interindividual differences. In contrast to Example 1, we did not specify an interaction between group and time predicting received support or physical activity adherence. Gender and baseline received support (grand-mean centered) were included as covariates at the between-person level as they have been shown to be associated with both mediator and outcome. The data from Example 2 had missing data. Forty-three of the 119 participants had fewer than 28 days of data, and five of these had fewer than 14 days of data. We used Mplus (version 8.4) to fit the RDSEM model, and it uses a Kalman filter approach to handle longitudinal missing data [22]. We reported the model with 3,000 iterations, but checked convergence with 6,000 iterations. The formal set of equations of this model, as well as data and Mplus syntax can be found at <https://osf.io/7vbeh/>.

Figure 8 summarizes the results, including the overall significant decrease in received support ($B = -0.03$, $SE = 0.01$, $p = .001$) and in physical activity adherence

($B = -0.04$, $SE = 0.01$, $p = .002$) over time in both groups. Participants in the intervention group showed significantly higher daily received support compared to participants in the control group ($B = 0.62$, $SE = 0.15$, $p < .001$). Higher received support on a given day was significantly associated with higher physical activity adherence that day ($B = 0.25$, $SE = 0.04$, $p < .001$). There was a significant indirect effect of the action control intervention on physical activity adherence via received support ($B = 0.15$, $SE = 0.05$, $p < .001$). Comparing this model with alternate models (e.g., specifying interactions between time and the effect of the intervention on received support) did not reveal any evidence for time interactions in the mediation paths (see <https://osf.io/7vbeh/>).

Conclusions

Example 2 contrasts with Example 1. Although a temporal effect on physical activity adherence and the mediating mechanism was observed (an overall decline), Steps 1–5 revealed no temporal variation in the mediation effect. Received support remained a constant mechanism of stable differences in physical activity adherence between the intervention and the control group. However, without the use of intensive longitudinal data, we could not have ruled out this possibility, and applying a more traditional mediation model (e.g., aggregating over time) might not have been adequate and led to wrong conclusions.

Discussion

Instead of carrying out a mediation analysis of an intervention's effect at single measurement times of M and Y, we recommend that researchers more explicitly consider the role of time when examining causal effects. Intensive longitudinal designs are particularly well suited allowing researchers to examine the temporal dynamics of the effects of interventions and their underlying mechanisms, but our approach can be used with as few as three measurements following the introduction of the intervention. Our empirical Examples 1 and 2 illustrate what can be learned about intervention processes when mediators and outcomes are measured at different times and are then systematically examined and modeled using the five conceptual and analytic steps we outlined above. Our two examples illustrated ways how the dynamics can differ from one intervention context to another. In the first example, the intervention seemed to change the trajectory of action control and the level of action control remained steadily related to healthy eating. In this example, however, the degree of mediation differed depending on the time point selected. In the second

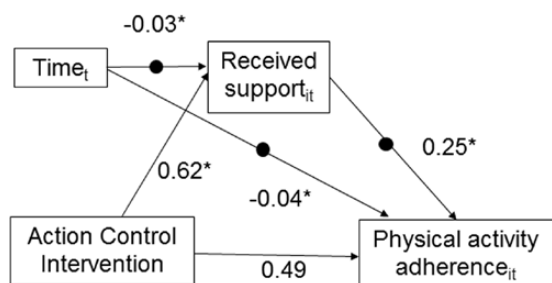


Fig. 8. Example 2. Residual dynamic structural equation mediation model of between-person intervention on social support and binary physical activity adherence, modeled with a probit link function. Black dots on three paths indicate that these are treated as random effects, differing systematically across individuals. i = individual, t = time.

example, the intervention seemed to have an immediate effect on the mediator received support and that effect did not change over time. Received support had a steady impact on the likelihood of physical activity adherence. In this example, the amount of the effect that is mediated seemed to be constant.

Neither example revealed systematic variation in the mediator–outcome relationship, and no evidence was found that the mediators might become more effective during the course of these interventions. Future studies should investigate to what extent this effect is replicable for other health-related cognitions and behaviors and to other domains of psychology and behavioral medicine.

In our examples, we used Steps 1–4 to examine the patterns in the data, but one could also think about these models conceptually and build a theory that predicts the temporal dynamics of the mediation process before collecting data (e.g., [7]). If there are temporal dynamics, the usual stability assumption may obscure a better understanding of the timing for causal processes for theory, design, and analysis. In line with dual-process models of behavior change (e.g., [34]), for example, the behavior change processes can be effortful (i.e., using self-regulation) or leading to automaticity and habit formation.

We chose to make the point about temporal variation with relatively simple mediations. There are many ways this approach can be extended. For example, it is often known that multiple mediators explain an effect. These may have nonsynchronous and nonlinear trajectories. In cases where the outcome improves but the mediator stagnates, this could indicate that the initial causal effect is substituted by another mechanism with its own temporal trajectory. Intensive longitudinal data offer a particularly unique insight into processes over and sequentially in time. For example, if healthy eating increases but action control stagnates, this could mean a transition from effortful regulation via action control to automatic regulation through habit or learning or a lasting change in the environment. In this example, action control may be the mediator of the intervention effect in the beginning and may then fade. In turn, habit may become the mediating mechanism later. Such hypotheses can be tested in the presented five-step approach by integrating multiple mediators and quadratic functions for nonlinear mediation over time.

The LMSEM and RDSEM analyses in this paper illustrate approaches to integrating time into mediation analyses, but other approaches may be more appropriate, depending on hypothesized mediating process or the speed of change in mediator and outcome. For example, if we assumed that the between-person variation in the trajectories of the mediator explain the intervention effect, this could be tested using an adaptation of the latent growth mediation model of O’Laughlin et al. [18].

Also, we assumed a relatively fast linear process between intervention, mediator, and outcome and, therefore, conducted same-day associations between mediators and outcomes. We assumed that the supportive messages in Example 1 promoted healthy eating while they were being perceived perhaps up to a few hours after. Similarly, in Example 2, we expected that text message reminders promoted better daily adherence to physical activity recommendations through specific supportive behaviors (e.g., suggesting an activity and freeing resources) that same day. In both examples, it seems highly unlikely that the effects of the mediators would last through the night until the next day. However, for other interventions or mediators, the speed of the process could be slower and the delay could be different for mediator and outcome, warranting lagged analyses with appropriate time windows. Time can also be nonlinear and include discontinuities that can be modeled with splines (see, e.g., in [14]). Last but not least, a wider range of autoregressive effects models could be employed if lagged effects were part of the assumed causal processes [8,24]. These could include sequential mediation processes (e.g., [25]), as well as vector autoregressive processes where the mediating process and outcome are dynamically interrelated following an intervention. These approaches, however, require relatively larger numbers of time points. When only three or four time points are available, the researcher can only examine relatively crude patterns of mediation stability and change.

Finally, mediation analysis cannot determine the causality of the mediator–outcome relationship. This is also true for intensive longitudinal mediation analysis. A prerequisite is, therefore, that the mediator is a plausible mechanism of the intervention effect. For our examples, there is theoretical and experimental literature supporting that social support (e.g., [35]) and self-regulation (e.g., [36]) causally affect health or health behavior. Of course, this does not mean that the mediators investigated here are the only plausible mechanisms. In fact, our preregistrations define multiple possible mediators. As this paper aims to illustrate the approach of intensive longitudinal mediation rather than a full explanation of the intervention effects, we opted for a simple mediation model here.

Conclusion

Intervention studies in health and behavioral sciences typically assess mediators and outcomes at one or two macrotime follow-ups and the interval length may or may not be explicitly justified. At the same time, technological advances have led to an increase in the use of intensive longitudinal data. As we have shown in this

paper, exploring mediation in an (intensive) longitudinal context allows important conceptual contributions of understanding mechanisms of change that would not be possible to make with sparser data. Learning to address time appropriately in mediation analyses is, therefore, invaluable and can drive important advances in psychological theory and intervention practice.

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Compliance with Ethical Standards

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Authors' Contributions C.B., J.I., G.S., & P.E.S. jointly generated the ideas represented in this paper. C.B. (physical activity trial) and J.I. (eating behavior trial) and U.S. (both trials) designed the empirical studies, and supervised the data collection. C.B., J.I. and P.E.S. wrote the analysis code and analyzed the data, and U.S. verified the accuracy of those analyses. C.B., J.I., G.S. and P.E.S. jointly wrote the first draft of the manuscript. All authors critically edited it, and approved the final submitted version of the manuscript.

Ethical Approval The respective institutional review boards (University of Zurich for the eating behavior trial and University of Bern for the physical activity trial) approved the study protocols. All procedures, including the informed consent process, were conducted in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2000

Informed Consent All participants included in the studies provided written informed consent.

References

- Baron RM, Kenny DA. The moderator-mediator variable distinction in social psychological research: Conceptual, strategic, and statistical considerations. *J Pers Soc Psychol.* 1986;51:1173–1182.
- Gu F, Preacher KJ, Ferrer E. A state space modeling approach to mediation analysis. *J Educ Behav Stat.* 2014;39(2):117–143.
- Judd CM, Kenny DA. Process analysis: Estimating mediation in treatment evaluations. *Eval Rev.* 1981;5(5):602–619.
- MacKinnon DP. *Introduction to Statistical Mediation Analysis.* New York, NY: Taylor & Francis Group/Lawrence Erlbaum Associates; 2008.
- Imai K, Keele L, Tingley D. A general approach to causal mediation analysis. *Psychol Methods.* 2010;15:309–334.
- Gollob HF, Reichardt CS. Taking account of time lags in causal models. *Child Dev.* 1987;58:80–92.
- Scholz U. It's time to think about time in health psychology. *Appl Psychol Health Well Being.* 2019;11:173–186.
- Cole DA, Maxwell SE. Testing mediational models with longitudinal data: Questions and tips in the use of structural equation modeling. *J Abnorm Psychol.* 2003;112:558–577.
- Maxwell SE, Cole DA. Bias in cross-sectional analyses of longitudinal mediation. *Psychol Methods.* 2007;12:23–44.
- Berli C, Stadler G, Inauen J, Scholz U. Action control in dyads: A randomized controlled trial to promote physical activity in everyday life. *Soc Sci Med.* 2016;163:89–97.
- Geschwind N, Peeters F, Drukker M, van Os J, Wichers M. Mindfulness training increases momentary positive emotions and reward experience in adults vulnerable to depression: A randomized controlled trial. *J Consult Clin Psychol.* 2011;79:618–628.
- Pepperell JC, Ramdassingh-Dow S, Crosthwaite N, et al. Ambulatory blood pressure after therapeutic and subtherapeutic nasal continuous positive airway pressure for obstructive sleep apnoea: A randomised parallel trial. *Lancet.* 2002;359:204–210.
- Hamaker EL, Wichers M. No time like the present: Discovering the hidden dynamics in intensive longitudinal data. *Curr Dir Psychol Sci.* 2017;26(1):10–15.
- Inauen J, Bolger N, Shrout PE, et al. Using smartphone-based support groups to promote healthy eating in daily life: A randomised trial. *Appl Psychol Health Well-Being.* 2017;9(3):303–323.
- Scholz U, Berli C. A dyadic action control trial in overweight and obese couples (DYACTIC). *BMC Public Health.* 2014;14:1321.
- Goldsmith KA, MacKinnon DP, Chalder T, White PD, Sharpe M, Pickles A. Tutorial: The practical application of longitudinal structural equation mediation models in clinical trials. *Psychol Methods.* 2018;23:191–207.
- Bauer DJ, Preacher KJ, Gil KM. Conceptualizing and testing random indirect effects and moderated mediation in multi-level models: New procedures and recommendations. *Psychol Methods.* 2006;11:142–163.
- O'Laughlin KD, Martin MJ, Ferrer E. Cross-sectional analysis of longitudinal mediation processes. *Multivariate Behav Res.* 2018;6:1–28.
- Zhao Y, Luo X. Granger mediation analysis of multiple time series with an application to functional magnetic resonance imaging. *Biometrics.* 2019;75:788–798.
- Bollen KA, Curran PJ. *Latent Curve Models: A Structural Equation Perspective.* Hoboken, NJ: John Wiley & Sons, Inc; 2005. doi:10.1002/0471746096.
- Preacher KJ, Zyphur MJ, Zhang Z. A general multilevel SEM framework for assessing multilevel mediation. *Psychol Methods.* 2010;15:209–233.
- McNeish D, Hamaker EL. A primer on two-level dynamic structural equation models for intensive longitudinal data in Mplus [published online ahead of print December 19, 2019]. *Psychol Methods.* 2019. doi:10.1037/met0000250.
- Asparouhov T, Muthén B. Comparison of models for the analysis of intensive longitudinal data. *Struct Equ Modeling.* 2020;27(2):275–297.

24. Lütkepohl H. *Introduction to Multiple Time Series Analysis*. Berlin: Springer Berlin Heidelberg; 1991. doi:[10.1007/978-3-662-02691-5](https://doi.org/10.1007/978-3-662-02691-5).
25. Tofighi D, Kelley K. Indirect effects in sequential mediation models: Evaluating methods for hypothesis testing and confidence interval formation. *Multivariate Behav Res*. 2020; 55(2):188–210:1–23. doi:[10.1080/00273171.2019.1618545](https://doi.org/10.1080/00273171.2019.1618545).
26. Bolger N, Laurenceau J-P. *Intensive Longitudinal Methods: An Introduction to Diary and Experience Sampling Research*. New York, NY: Guilford Press; 2013.
27. Schafer JL, Graham JW. Missing data: Our view of the state of the art. *Psychol Methods*. 2002;7:147–177.
28. Sniehotta FF, Scholz U, Schwarzer R. Bridging the intention–behaviour gap: Planning, self-efficacy, and action control in the adoption and maintenance of physical exercise. *Psychol Health*. 2005;20(2):143–160.
29. Curran PJ, Bauer DJ. The disaggregation of within-person and between-person effects in longitudinal models of change. *Annu Rev Psychol*. 2011;62:583–619.
30. Pituch KA, Stapleton LM. Distinguishing between cross- and cluster-level mediation processes in the cluster randomized trial. *Soc Methods Res*. 2012;41(4):630–670.
31. Shrout PE, Bolger N. Mediation in experimental and nonexperimental studies. *Psychol Methods*. 2002;7(4):422–445.
32. Berli C, Stadler G, Shrout PE, Bolger N, Scholz U. Mediators of physical activity adherence: Results from an action control intervention in couples. *Ann Behav Med*. 2018;52:65–76.
33. MacKinnon DP, Dwyer JH. Estimating mediated effects in prevention studies. *Eval Rev*. 1993;17(2):144–158.
34. Strack F, Deutsch R. Reflective and impulsive determinants of social behavior. *Pers Soc Psychol Rev*. 2004;8:220–247.
35. Kirsch JA, Lehman BJ. Comparing visible and invisible social support: Non-evaluative support buffers cardiovascular responses to stress. *Stress Health*. 2015;31:351–364.
36. Hofmann W, Friese M, Roefs A. Three ways to resist temptation: The independent contributions of executive attention, inhibitory control, and affect regulation to the impulse control of eating behavior. *J Exp Soc Psychol*. 2009;45(2):431–435.